10/009930

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PASSWORD:
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LOGINID:ssspta1813nxm

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS, LIFESCI, CAPLUS' AT 15:52:35 ON 23 JUL 2003
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FULL ESTIMATED COST	24.38	24.59

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=> d his

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     FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
     LIFESCI, CAPLUS' ENTERED AT 15:42:05 ON 23 JUL 2003
                E HARDER ACHIM/AU
L1           139 S E3
                E VON SAMSON-HIMMELSTJERNA GEORG/AU
L2             2 S E4

=> e von samson georg/au
E1            34      VON SAMSON E/AU
E2             1      VON SAMSON G/AU
E3             0 --> VON SAMSON GEORG/AU
E4             1      VON SAMSON H/AU
E5             1      VON SAMSON HIMELSTJERNA G/AU
E6             1      VON SAMSON HIMELSTJERNA GEORG/AU
E7             1      VON SAMSON HIMMEL ST JERNA G/AU
E8             1      VON SAMSON HIMMELSRJEMA G/AU
E9             1      VON SAMSON HIMMELST JERNA G/AU
E10            1      VON SAMSON HIMMELSTJERNA A/AU
E11          101      VON SAMSON HIMMELSTJERNA G/AU
E12           45      VON SAMSON HIMMELSTJERNA GEORG/AU

=> e
E13            3      VON SAMSON HIMMELSTJERNA H O/AU
E14            7      VON SAMSON HIMMELSTJERNA M/AU
E15            3      VON SAMSON HIMMELSTJERNA M C/AU
E16            4      VON SAMSON HIMMELSTJERNA MATTHIAS/AU
E17            1      VON SAMSON HIMMESTJERNA M/AU
E18            1      VON SAMSON HIMMESTJERNA MATTHIAS/AU
E19            2      VON SAMSON JOERG/AU
E20            7      VON SAMSON P/AU
E21            7      VON SAMSON PATRICK/AU
E22            1      VON SAMSON V E/AU
E23            2      VON SAMSONHIMMELSTJERNA G/AU
E24            1      VON SAMSONOW ALEXANDER/AU

=> s e2-e12
L3           149 ("VON SAMSON G"/AU OR "VON SAMSON GEORG"/AU OR "VON SAMSON H"/AU
                  OR "VON SAMSON HIMELSTJERNA G"/AU OR "VON SAMSON HIMELSTJERNA
                 GEORG"/AU OR "VON SAMSON HIMMEL ST JERNA G"/AU OR "VON SAMSON
                 HIMMELSRJEMA G"/AU OR "VON SAMSON HIMMELST JERNA G"/AU OR "VON
                 SAMSON HIMMELSTJERNA A"/AU OR "VON SAMSON HIMMELSTJERNA G"/AU
                 OR "VON SAMSON HIMMELSTJERNA GEORG"/AU)

=> s e23
L4             2 "VON SAMSONHIMMELSTJERNA G"/AU

=> s l1-l4
L5           256 (L1 OR L2 OR L3 OR L4)

=> s l5 and endoparasit?
L6            62 L5 AND ENDOPARASIT?

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7            55 DUP REM L6 (7 DUPLICATES REMOVED)

=> s l7 and depsideptide
L8             0 L7 AND DEPSIDEPTIDE
```

=> s l7 and depsipeptide
L9 14 L7 AND DEPSIPEPTIDE

=> d bib ab 1-14

L9 ANSWER 1 OF 14 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-629043 [68] WPIDS
DNC C2002-177712
TI Use of **depsipeptide** for control of **endoparasites**, e.g. cestodes, trematodes, nematodes or acantocephalans, as solid in specific crystal modification.
DC B03 C02
IN HARDER, A; KALBE, J; TRAEUBEL, M; **VON SAMSON-HIMELSTJERNA, G**; **VON SAMSON-HIMMELSTJERNA, G**
PA (FARB) BAYER AG
CYC 100
PI DE 10104362 A1 20020808 (200268)* 6p
WO 2002066048 A1 20020829 (200268) DE
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
ADT DE 10104362 A1 DE 2001-10104362 20010201; WO 2002066048 A1 WO 2002-EP541 20020121
PRAI DE 2001-10104362 20010201
AB DE 10104362 A UPAB: 20021022
NOVELTY - Use of a specific **depsipeptide** (I), as a solid in crystal modification I.
DETAILED DESCRIPTION - Use of a specific **depsipeptide** of formula (I), as a solid in crystal modification I.
ACTIVITY - Antiparasitic.
Sheep were infected with 5000 L3 larvae of Haemonchus contortus, then treated with 0.1 mg/kg (orally in a gelatine capsule) of (I) as crystal modification I.
Anthelmintic activity, as measured from the number of worm eggs in the feces, was over 95%. Similar doses of other crystal modifications were less effective with activity 75% or lower.
MECHANISM OF ACTION - None given in the source material.
USE - (I) is used for control (treatment or prevention) of **endoparasites**, e.g. cestodes, trematodes, nematodes or acantocephalans, in humans and other animals (e.g. mammals, birds, fish, reptiles or insects), and is active against all, or individual, stages of the life cycle, of normally sensitive or resistant strains.
ADVANTAGE - Crystal modification I has greater bioavailability, and thus activity, than other modifications.
Dwg.0/0

L9 ANSWER 2 OF 14 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-076332 [11] WPIDS
DNC C2002-023023
TI Article for oral administration of veterinary drugs, especially **depsipeptide endoparasiticides**, comprising aroma-containing starch-based extrudate, is readily accepted by animals such as dogs.
DC B03 C02
IN GEISSLER, K; HARDER, A; KALBE, J; TRAEUBEL, M; **VON SAMSON-HIMMELSTJERNA, G**
PA (FARB) BAYER AG
CYC 97

PI DE 10031044 A1 20020103 (200211)* 11p
WO 2002000202 A1 20020103 (200211) DE
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001079664 A 20020108 (200235)
NO 2002006209 A 20030123 (200320)
CZ 2002004141 A3 20030312 (200324)
EP 1296655 A1 20030402 (200325) DE
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
BR 2001011914 A 20030513 (200335)
KR 2003023874 A 20030320 (200346)
ADT DE 10031044 A1 DE 2000-10031044 20000626; WO 2002000202 A1 WO 2001-EP6836 20010618; AU 2001079664 A AU 2001-79664 20010618; NO 2002006209 A WO 2001-EP6836 20010618, NO 2002-6209 20021223; CZ 2002004141 A3 WO 2001-EP6836 20010618, CZ 2002-4141 20010618; EP 1296655 A1 EP 2001-957856 20010618, WO 2001-EP6836 20010618; BR 2001011914 A BR 2001-11914 20010618, WO 2001-EP6836 20010618; KR 2003023874 A KR 2002-717197 20021217
FDT AU 2001079664 A Based on WO 200200202; CZ 2002004141 A3 Based on WO 200200202; EP 1296655 A1 Based on WO 200200202; BR 2001011914 A Based on WO 200200202
PRAI DE 2000-10031044 20000626
AB DE 10031044 A UPAB: 20020215
NOVELTY - A starch-based extruded shaped article (A) contains special aromas, consistency-providing agents and veterinary drugs (I).
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the preparation of (A), by mixing the components and further processing at temperatures below 150 deg. C.
USE - (A) is useful for the administration of oral adminstration of (I) to animals such as dogs, cats or horses. (I) are specifically cyclic depsipeptides (I'), consisting of aminoacid and hydroxycarboxylic acid units and having 6-30 ring or chain atoms (claimed). (I') are **endoparasiticides** (for therapeutic or prophylactic use), described e.g. in EP382173, DE4317432, DE4317457 and DE4317458.
ADVANTAGE - (A) is readily accepted by and palatable to animals. Addition of meat is unnecesary. (A) is readily prepared by conventional extrusion, and provides a simple method of administration of (I).
Dwg.0/0

L9 ANSWER 3 OF 14 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2001-523377 [58] WPIDS
DNC C2001-156416
TI **Endoparasiticide** composition effective on topical administration, comprises solution of **depsipeptide** in solvent such as 1,2-isopropylidene-glycerol.
DC B03 C02
IN HARDER, A; KALBE, J; MENCKE, N; STEGEMANN, M; TRAEUBEL, M; **VON SAMSON-HIMMELST JERNA, G**; **VON SAMSON-HIMMELSTJERNA, G**; TRAUBEL, M; **VON-SAMSON-HIMMELSTJERNA, G**
PA (FARB) BAYER AG; (HARD-I) HARDER A; (KALB-I) KALBE J; (MENC-I) MENCKE N; (STEG-I) STEGEMANN M; (TRAU-I) TRAUBEL M; (VONS-I) VON-SAMSON-HIMMELSTJERNA G
CYC 95
PI DE 10008128 A1 20010823 (200158)* 10p
WO 2001062268 A1 20010830 (200158) DE
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC

LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001040605 A 20010903 (200202)
BR 2001008562 A 20021112 (200281)
NO 2002003976 A 20021021 (200281)
EP 1259250 A1 20021127 (200302) DE
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR
CZ 2002002867 A3 20030115 (200309)
KR 2002072577 A 20020916 (200311)
HU 2002004554 A2 20030528 (200341)
CN 1404397 A 20030319 (200344)
US 2003125244 A1 20030703 (200345)

ADT DE 10008128 A1 DE 2000-10008128 20000222; WO 2001062268 A1 WO 2001-EP1392 20010209; AU 2001040605 A AU 2001-40605 20010209; BR 2001008562 A BR 2001-8562 20010209, WO 2001-EP1392 20010209; NO 2002003976 A WO 2001-EP1392 20010209, NO 2002-3976 20020821; EP 1259250 A1 EP 2001-911623 20010209, WO 2001-EP1392 20010209; CZ 2002002867 A3 WO 2001-EP1392 20010209, CZ 2002-2867 20010209; KR 2002072577 A KR 2002-710032 20020803; HU 2002004554 A2 WO 2001-EP1392 20010209, HU 2002-4554 20010209; CN 1404397 A CN 2001-805400 20010209; US 2003125244 A1 WO 2001-EP1392 20010209, US 2002-204880 20020822

FDT AU 2001040605 A Based on WO 200162268; BR 2001008562 A Based on WO 200162268; EP 1259250 A1 Based on WO 200162268; CZ 2002002867 A3 Based on WO 200162268; HU 2002004554 A2 Based on WO 200162268

PRAI DE 2000-10008128 20000222

AB DE 10008128 A UPAB: 20011010

NOVELTY - Composition (A) containing a cyclic **depsipeptide** (I) (optionally together with other active agents) additionally contains at least one solvent (II) and is formulated for topical administration to animals.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the preparation of (A), by mixing (I) with (II) and optionally further additives.

ACTIVITY - Antiparasitic; anthelmintic.

A solution of 5 wt.% **depsipeptide** (unspecified) in 66.5 wt. % isopropylidene glycerol and 28.5 wt. % benzyl alcohol gave 100% control of Toxocara canis and Ancylostoma caninum in dogs and Toxocara cati in cats within 2-4 days at a **depsipeptide** dosage of 5 mg/kg.

MECHANISM OF ACTION - None given.

USE - (A) are used as **endoparasiticides** (claimed). They are useful for therapeutic or prophylactic control of a broad spectrum of **endoparasites** (including cestodes, trematodes, nematodes and acanthocephalae) in animals such as cats or dogs. Use in humans is also possible.

ADVANTAGE - In the form of (A), (I) are highly effective on topical/transdermal administration in controlling **endoparasites** in the gastrointestinal tract, despite the fact that molecules (especially peptides) of molecular weight more than 1000 usually show poor skin penetration on topical administration. The preparations (A) also have good long-term stability.

Dwg.0/0

L9 ANSWER 4 OF 14 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2001-041784 [06] WPIDS
DNC C2001-012205
TI Synergistic ectoparasiticide combination for use in human or veterinary medicine, comprising cyclic **depsipeptide** and piperazine compound as potentiating agent.
DC B03 C02
IN HARDER, A; SAMSON-HIMMELSTJERNA, G; **VON SAMSON-HIMMELSTJERNA, G**
PA (FARB) BAYER AG
CYC 93

PI DE 19921887 A1 20001116 (200106)* 15p
WO 2000069425 A2 20001123 (200106) DE
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000055237 A 20001205 (200113)
BR 2000010499 A 20020213 (200220)
NO 2001005398 A 20011105 (200222)
SK 2001001626 A3 20020305 (200225)
EP 1189615 A2 20020327 (200229) DE
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
KR 2001109527 A 20011210 (200237)
CZ 2001004060 A3 20020612 (200251)
CN 1352559 A 20020605 (200261)
HU 2002001201 A2 20020828 (200264)
ZA 2001008238 A 20021224 (200309) 51p
JP 2002544224 W 20021224 (200313) 46p

ADT DE 19921887 A1 DE 1999-19921887 19990512; WO 2000069425 A2 WO 2000-EP4014 20000504; AU 2000055237 A AU 2000-55237 20000504; BR 2000010499 A BR 2000-10499 20000504, WO 2000-EP4014 20000504; NO 2001005398 A WO 2000-EP4014 20000504, NO 2001-5398 20011105; SK 2001001626 A3 WO 2000-EP4014 20000504, SK 2001-1626 20000504; EP 1189615 A2 EP 2000-940235 20000504, WO 2000-EP4014 20000504; KR 2001109527 A KR 2001-713555 20011023; CZ 2001004060 A3 WO 2000-EP4014 20000504, CZ 2001-4060 20000504; CN 1352559 A CN 2000-807450 20000504; HU 2002001201 A2 WO 2000-EP4014 20000504, HU 2002-1201 20000504; ZA 2001008238 A ZA 2001-8238 20011008; JP 2002544224 W JP 2000-617884 20000504, WO 2000-EP4014 20000504

FDT AU 2000055237 A Based on WO 200069425; BR 2000010499 A Based on WO 200069425; SK 2001001626 A3 Based on WO 200069425; EP 1189615 A2 Based on WO 200069425; CZ 2001004060 A3 Based on WO 200069425; HU 2002001201 A2 Based on WO 200069425; JP 2002544224 W Based on WO 200069425

PRAI DE 1999-19921887 19990512

AB DE 19921887 A UPAB: 20021105

NOVELTY - The use of piperazine derivatives (I) is claimed for potentiating the **endoparasitic** activity of cyclic depsipeptides (II), consisting of aminoacids and hydroxycarboxylic acids as ring components and having 24 ring atoms.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(i) **endoparasitic** compositions containing (I) and (II); and

(ii) the use of (I) together with (II) for the preparation of **endoparasitic** compositions.

ACTIVITY - Anthelmintic.

In tests against Heterakis spumosa in mice, piperazine (Ia) at 4 x 250 mg/kg alone or '**depsipeptide** I' (IIa) (see WO9325543) at 4 x 1 mg/kg alone gave 50-75% worm reduction, whereas a combination of (Ia) at 4 x 250 mg/kg and (IIa) at 4 x 1 mg/kg gave complete (more than 90%) worm reduction.

MECHANISM OF ACTION - None given.

USE - The combinations of (I) and (II) are useful in human or veterinary medicine for controlling pathogenic **endoparasites**, specifically cestodes, trematodes, nematodes or acanthocephalae. Activity is demonstrated in tests against Trichinella spiralis in vitro and against Heterakis spumosa or Nematospiroides dibius in mice.

ADVANTAGE - The combination of (I) and (II) (both known ectoparasiticides) has synergistic action, due to potentiation of the activity of (II) by (I).

Dwg.0/0

L9 ANSWER 5 OF 14 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 1998-532765 [46] WPIDS
DNC C1998-159906
TI New cyclic thio-**depsipeptide**(s) - useful for controlling **endoparasites**.
DC B04 C03
IN BONSE, G; HARDER, A; JESCHKE, P; LINUMA, K; MENCKE, N; SAKANAKA, O; **VON SAMSON-HIMMELSTJERNA, G**; IINUMA, K; **VON SAMSON, G**; **VON SAMSON HIMMELSTJERNA, G**; SAMSON-HIMMELSTJERNA, G V
PA (FARB) BAYER AG; (MEIJ) MEIJI SEIKA KAISHA LTD
CYC 82
PI DE 19713626 A1 19981008 (199846)* 26p
WO 9843965 A1 19981008 (199846) DE
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9870388 A 19981022 (199910)
EP 973756 A1 20000126 (200010) DE
R: CH DE ES FR GB IT LI NL
CN 1259128 A 20000705 (200052)
NZ 338102 A 20010223 (200115)
AU 731789 B 20010405 (200125)
KR 2000076392 A 20001226 (200134)
US 6265537 B1 20010724 (200146)
JP 2001524952 W 20011204 (200203) 83p
EP 973756 B1 20030326 (200323) DE
R: CH DE ES FR GB IT LI NL
DE 59807652 G 20030430 (200330)
ADT DE 19713626 A1 DE 1997-19713626 19970402; WO 9843965 A1 WO 1998-EP1628 19980320; AU 9870388 A AU 1998-70388 19980320; EP 973756 A1 EP 1998-917025 19980320, WO 1998-EP1628 19980320; CN 1259128 A CN 1998-805729 19980320; NZ 338102 A NZ 1998-338102 19980320, WO 1998-EP1628 19980320; AU 731789 B AU 1998-70388 19980320; KR 2000076392 A WO 1998-EP1628 19980320, KR 1999-708495 19990917; US 6265537 B1 WO 1998-EP1628 19980320, US 1999-381946 19990927; JP 2001524952 W JP 1998-541108 19980320, WO 1998-EP1628 19980320; EP 973756 B1 EP 1998-917025 19980320, WO 1998-EP1628 19980320; DE 59807652 G DE 1998-507652 19980320, EP 1998-917025 19980320, WO 1998-EP1628 19980320
FDT AU 9870388 A Based on WO 9843965; EP 973756 A1 Based on WO 9843965; NZ 338102 A Based on WO 9843965; AU 731789 B Previous Publ. AU 9870388, Based on WO 9843965; KR 2000076392 A Based on WO 9843965; US 6265537 B1 Based on WO 9843965; JP 2001524952 W Based on WO 9843965; EP 973756 B1 Based on WO 9843965; DE 59807652 G Based on EP 973756, Based on WO 9843965
PRAI DE 1997-19713626 19970402
AB DE 19713626 A UPAB: 19981118
Cyclic thiodepsipeptides of formula (I), their optical isomers and racemates are new: where R1, R4, R7 and R10 = H or 1-4C alkyl; R2, R5, R8, R11 = H or optionally substituted 1-8C alkyl, 2-8C alkenyl, 3-6C cycloalkyl, (3-6C)cycloalkyl-(1-2C)alkyl, aryl-(1-2C)alkyl, heteroaryl-(1-2C)alkyl, aryl or heteroaryl; or R10+R11 complete a 5- or 6-membered ring that is optionally interrupted by O, S, SO or SO2 and optionally substituted; R3, R9 = H, 1-8C alkyl, aryl-(1-2C)alkyl or (3-6C)cycloalkyl-(1-2C)alkyl; R6, R12 = H or optionally substituted 1-8C alkyl, 2-8C alkenyl, 3-6C cycloalkyl, (3-6C)cycloalkyl-(1-2C)alkyl, aryl-(1-2C)alkyl, heteroaryl-(1-2C)alkyl, aryl or heteroaryl; X1-X4 = O or S, at least one being S.

USE - for controlling **endoparasites** that infest humans and other animals, including cestodes, trematodes, nematodes and acanthocephalids.

Dwg.0/0

L9 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:819404 CAPLUS
DN 132:36040
TI Synthesis of sulfonyl-substituted cyclooctadepsipeptides for use in combating **endoparasites**
IN Scherkenbeck, Jurgen; Dyker, Hubert; Plant, Andrew; **Harder, Achim**; **Von Samson Himmelstjerna, Georg**
PA Bayer A.-G., Germany
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9967281	A1	19991229	WO 1999-EP4028	19990611
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19828047	A1	19991230	DE 1998-19828047	19980624
CA 2332122	AA	19991229	CA 1999-2332122	19990611
AU 9945114	A1	20000110	AU 1999-45114	19990611
BR 9911574	A	20010320	BR 1999-11574	19990611
EP 1090031	A1	20010411	EP 1999-927953	19990611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
JP 2002518520	T2	20020625	JP 2000-555932	19990611
PRAI DE 1998-19828047	A	19980624		
WO 1999-EP4028	W	19990611		

OS MARPAT 132:36040
AB The invention relates to new substituted cyclooctadepsipeptides [(I); R, R1 = SO2-A in 2- or 4-position; A = NR2R3; R2, R3 = (independently) H, (substituted)alkyl; m = 1 - 2; n = 0 - 2], a method for their prepn. and their use for fighting **endoparasites**, as well as drugs contg. them as active ingredients. Thus, **depsipeptide** PF 1022 was reacted with chlorosulfonic acid, and the product further reacted with substituted amines (no data), to give the desired products. In in vivo tests using sheep infected with H. contortus, eight test compds. all resulted in >95% redn. of infection at 0.05 mg/kg p.o.; against T. colubriformis, four test compds. resulted in >95% redn. of infection at 0.25 mg/kg p.o.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:51502 CAPLUS
DN 126:84585
TI **Endoparasitic** drug combination
IN Mencke, Norbert; **Harder, Achim**; Jeschke, Peter; Helpap, Barbara
PA Bayer A.-G., Germany
SO Ger. Offen., 17 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 19520275	A1	19961205	DE 1995-19520275	19950602

	TW 469133	B	20011221	TW 1996-85105513	19960510
	CA 2222680	AA	19961205	CA 1996-2222680	19960520
	WO 9638165	A2	19961205	WO 1996-EP2170	19960520
	WO 9638165	A3	19970109		
	W: AU, BB, BG, BR, BY, CA, CN, CZ, HU, JP, KR, KZ, LK, MX, NO, NZ, PL, RO, RU, SK, TR, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9659004	A1	19961218	AU 1996-59004	19960520
	AU 703048	B2	19990311		
	EP 828506	A2	19980318	EP 1996-916137	19960520
	EP 828506	B1	20020227		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
	CN 1191489	A	19980826	CN 1996-195661	19960520
	JP 11506438	T2	19990608	JP 1996-536146	19960520
	BR 9608961	A	19990629	BR 1996-8961	19960520
	CZ 287290	B6	20001011	CZ 1997-3825	19960520
	AT 213645	E	20020315	AT 1996-916137	19960520
	ES 2173284	T3	20021016	ES 1996-916137	19960520
	PL 184848	B1	20021231	PL 1996-323595	19960520
	IL 118518	A1	19981227	IL 1996-118518	19960531
	US 6159932	A	20001212	US 1997-952356	19971119
	NO 9705516	A	19980106	NO 1997-5516	19971201
PRAI	DE 1995-19520275	A	19950602		
	WO 1996-EP2170	W	19960520		

OS MARPAT 126:84585

AB A combination of a macrocyclic lactone (avermectin, ivermectin, or milbemycin) with a cyclic **depsipeptide**, optionally including praziquantel or epsiprantel, is useful as a synergistic nematocide for treatment of ascarid, hookworm, trichurid, and filarial infestations in mammals. Thus, a combination of PF 1022A (cyclic **depsipeptide**) 50.0 and ivermectin B1a/B1b 0.1 mg/kg orally was 100% effective against Nematospiroides dubius infestation in mice.

L9 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1996:379698 CAPLUS

DN 125:59134

TI Aromatic sulfonylation, sulfenylation, thiocyanation, and phosphorylation of cyclic depsipeptides in preparation of **endoparasiticides**.

IN Scherkenbeck, Juergen; Plant, Andrew; Jeschke, Peter; **Harder, Achim**; Mencke, Norbert

PA Bayer A.-G., Germany

SO Ger. Offen., 15 pp.
CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4437198	A1	19960425	DE 1994-4437198	19941018
	CA 2202751	AA	19960425	CA 1995-2202751	19951005
	WO 9611945	A2	19960425	WO 1995-EP3926	19951005
	W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KR, KZ, LK, MX, NO, NZ, PL, RO, RU, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9538038	A1	19960506	AU 1995-38038	19951005
	AU 698898	B2	19981112		
	EP 787141	A2	19970806	EP 1995-935902	19951005
	EP 787141	B1	20000830		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
	CN 1162961	A	19971022	CN 1995-195746	19951005
	BR 9509377	A	19971118	BR 1995-9377	19951005

	HU 77019	A2	19980302	HU 1997-2045	19951005
	HU 218569	B	20001028		
	JP 10511341	T2	19981104	JP 1995-512897	19951005
	AT 195952	E	20000915	AT 1995-935902	19951005
	ES 2149378	T3	20001101	ES 1995-935902	19951005
	US 5874530	A	19990223	US 1997-817279	19970410
	FI 9701610	A	19970416	FI 1997-1610	19970416
PRAI	DE 1994-4437198	A	19941018		
	WO 1995-EP3926	W	19951005		

OS MARPAT 125:59134

AB Title processes are carried out on cyclic depsipeptides prepd. from .alpha.-hydroxycarboxylic acids and .alpha.-amino acids and contg. 6-24 ring atoms and .gtoreq.1 Ph ring using the appropriate reagents, optionally in the presence of catalysts, additives, and/or diluents. Cyclic depsipeptides [I; .gtoreq.1 of R3-R10 = sulfonylated, sulfenylated, thiocyanated, or phosphorylated Ph, PhCH2; R1, R2, R11, R12 = H, (substituted) alkyl, cycloalkyl, aralkyl, aryl; R3, R5, R7, R9 = H, (substituted) alkyl; R4, R6, R8, R10 = H, (substituted) alkyl, alkenyl, cycloalkyl, aryl, aralkyl], useful as **endoparasiticides**, are claimed. I (R1, R2, R5, R9, R11, R12 = Me; R4, R6, R8, R10 = CH2CHMe2; R3, R7 = morpholine-4-sulfonyl) was effective against Hemonchus contortus in sheep at 0.5 mg/kg.

L9 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1995:951170 CAPLUS

DN 124:9453

TI Preparation of cyclic depsipeptides as **endoparasiticides**

IN Scherkenbeck, Juergen; Jeschke, Peter; Plant, Andrew; **Harder, Achim**; Mencke, Norbert

PA Bayer A.-G., Germany

SO Ger. Offen., 31 pp.
CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4401389	A1	19950720	DE 1994-4401389	19940119
	EP 664297	A1	19950726	EP 1995-100198	19950109
	EP 664297	B1	19980408		
	ES 2115269	T3	19980616	ES 1995-100198	19950109
	JP 07206897	A2	19950808	JP 1995-21325	19950113
	US 5663140	A	19970902	US 1995-372543	19950113
PRAI	DE 1994-4401389		19940119		

OS MARPAT 124:9453

AB Title compds. [I; R1,R4 = H, (cyclo)alkyl, (hetero)aryl(alkyl), etc.; R2,R3,R5,R6 = H, (un)substituted alkyl, alkenyl, (hetero)aryl(alkyl), etc.] were prepd. Thus, prepd. I (R1 = R3 = R4 = R6 = Me, R2 = R5 = CMe3) had ED of 10mg/kg orally and/or i.v. against Haemonchus contortus in sheep.

L9 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1995:913288 CAPLUS

DN 123:340963

TI Preparation of cyclic depsipeptides having 18 ring atoms as **endoparasiticides**.

IN Jeschke, Peter; Scherkenbeck, Juergen; Bonse, Gerhard; Bischoff, Erwin; Mencke, Norbert; **Harder, Achim**; Londershausen, Michael; Mueller, Hartwig

PA Bayer A.-G., Germany

SO Eur. Pat. Appl., 42 pp.
CODEN: EPXXDW

DT Patent

LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 658551	A1	19950621	EP 1994-119130	19941205
	EP 658551	B1	19990519		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE				
	DE 4342907	A1	19950622	DE 1993-4342907	19931216
	AT 180254	E	19990615	AT 1994-119130	19941205
	ES 2133153	T3	19990901	ES 1994-119130	19941205
	JP 07196687	A2	19950801	JP 1994-331022	19941209
	US 5624897	A	19970429	US 1994-353409	19941209
	CA 2137961	AA	19950617	CA 1994-2137961	19941213
	AU 9480410	A1	19950622	AU 1994-80410	19941213
	AU 679585	B2	19970703		
	ZA 9410011	A	19950824	ZA 1994-10011	19941215
PRAI	DE 1993-4342907		19931216		

OS CASREACT 123:340963; MARPAT 123:340963
AB Title compds. [I; R = H, (cyclo)alkyl], were prepd. Thus, N-methylalanyl-D-lactyl-N-methylisoleucyl-D-lactyl-N-methylleucyl-D-lactic acid (prepn. given) was stirred with (Me2CH)2NEt and bis(2-oxo-3-oxazolidinyl)phosphonic acid chloride in CH2Cl2 at 0.degree. to room temp. to give 59.8% title compd. (II). II was effective against Trichostrongylus colubriformis and Haemonchus contortus in sheep at 10 mg/kg orally or i.v.

L9 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:813210 CAPLUS
DN 124:53819
TI Cyclic depsipeptides containing lactic acid with 18 ring atoms as **endoparasiticidal** agents and process for their preparation
IN Jeschke, Peter; **Harder, Achim**; Mencke, Norbert; Kleinkauf, Horst; Zocher, Rainer
PA Bayer A.-G., Germany
SO Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 669343	A1	19950830	EP 1995-101909	19950213
	EP 669343	B1	20030115		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
	DE 4406025	A1	19950831	DE 1994-4406025	19940224
	AT 231164	E	20030215	AT 1995-101909	19950213
	ES 2185671	T3	20030501	ES 1995-101909	19950213
	US 5656464	A	19970812	US 1995-390326	19950217
	CA 2143045	AA	19950825	CA 1995-2143045	19950221
	AU 9512387	A1	19950831	AU 1995-12387	19950221
	AU 689179	B2	19980326		
	JP 07252297	A2	19951003	JP 1995-55279	19950221
	FI 9500823	A	19950825	FI 1995-823	19950222
	NO 9500669	A	19950825	NO 1995-669	19950222
	PL 180162	B1	20001229	PL 1995-307415	19950222
	BR 9500757	A	19951024	BR 1995-757	19950223
	CN 1112932	A	19951206	CN 1995-102287	19950223
	ZA 9501524	A	19951208	ZA 1995-1524	19950223
	HU 72399	A2	19960429	HU 1995-555	19950223
	HU 219830	B	20010828		
	CZ 287506	B6	20001213	CZ 1995-482	19950223
	US 5945316	A	19990831	US 1997-821633	19970320
PRAI	DE 1994-4406025	A	19940224		

US 1995-390326 A3 19950217
OS MARPAT 124:53819
AB A process for the prodn. of optically active cyclic depsipeptides with 18 ring atoms by use of fungi of the genus Fusarium or their isolated enzyme prepns. is claimed.

L9 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:763739 CAPLUS
DN 123:179457
TI **Endoparasiticidal** agents containing praziquantel or epsiprantel and cyclic depsipeptides
IN Mencke, Norbert; **Harder, Achim**; Jeschke, Peter
PA Bayer A.-G., Germany
SO Eur. Pat. Appl., 39 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 662326	A2	19950712	EP 1994-120772	19941227
	EP 662326	A3	19971217		
	EP 662326	B1	20011128		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
	DE 4400464	A1	19950713	DE 1994-4400464	19940111
	AU 9481592	A1	19950720	AU 1994-81592	19941220
	AU 685535	B2	19980122		
	AT 209501	E	20011215	AT 1994-120772	19941227
	ES 2168285	T3	20020616	ES 1994-120772	19941227
	US 5589503	A	19961231	US 1995-368515	19950104
	FI 9500091	A	19950712	FI 1995-91	19950109
	JP 07223951	A2	19950822	JP 1995-16335	19950109
	IL 112285	A1	19990620	IL 1995-112285	19950109
	PL 180019	B1	20001229	PL 1995-306709	19950109
	NO 9500093	A	19950712	NO 1995-93	19950110
	HU 69180	A2	19950828	HU 1995-65	19950110
	ZA 9500136	A	19950907	ZA 1995-136	19950110
	CZ 290246	B6	20020612	CZ 1995-61	19950110
	CN 1121429	A	19960501	CN 1995-101158	19950111
	RU 2124364	C1	19990110	RU 1995-100759	19950111
PRAI	DE 1994-4400464	A	19940111		

OS MARPAT 123:179457
AB Praziquantel and epsiprantel enhance the **endoparasiticidal** action of cyclic depsipeptides. Thus, a 1:1 combination of praziquantel and cyclo(N-methyl-L-leucyl-D-lactoyl-N-methyl-L-leucyl-D-.beta.-phenyllactoyl-N-methyl-L-leucyl-D-lactoyl-N-methyl-L-leucyl-D-.beta.-phenyllactoyl) (PF 1022) was 100% effective against exptl. infestation with Ancylostoma caninum in dogs. Syntheses of cyclic depsipeptides with 18 and 24 ring atoms and their linear precursors is described.

L9 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:374823 CAPLUS
DN 122:160697
TI Preparation of octacyclodepsipeptides as **endoparasiticides**
IN Scherkenbeck, Juergen; Jeschke, Peter; Lerchen, Hans-Georg; Hagemann, Hermann; **Harder, Achim**; Mencke, Norbert; Plant, Andrew
PA Bayer A.-G., Germany
SO Eur. Pat. Appl., 46 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	EP 626375	A1	19941130	EP 1994-107543	19940516
	EP 626375	B1	20020605		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, SE				
	DE 4317457	A1	19941201	DE 1993-4317457	19930526
	AU 9460642	A1	19941201	AU 1994-60642	19940421
	AU 682847	B2	19971023		
	AT 218555	E	20020615	AT 1994-107543	19940516
	ES 2177555	T3	20021216	ES 1994-107543	19940516
	US 6369028	B1	20020409	US 1994-246029	19940519
	CA 2124059	AA	19941127	CA 1994-2124059	19940520
	JP 06340695	A2	19941213	JP 1994-129930	19940520
	ZA 9403638	A	19950126	ZA 1994-3638	19940525
	US 5777075	A	19980707	US 1995-510084	19950801
PRAI	DE 1993-4317457	A	19930526		
	US 1994-246029	A3	19940519		

OS MARPAT 122:160697

AB Title compds. [I; R1, R2, R11, R12 = (cyclo)alkyl, haloalkyl, aryl(alkyl); R3,R5,R7,R9 = H, alkyl, aryl(alkyl), etc.; R4, R6, R8, R10 = H, alk(en)yl, aryl(alkyl), etc.] were prepd. Thus, I (R1 = R2 = R5 = R9 = R11 = R12 = Me, R3 = R7 = CH2Ph, R4 = R6 = R8 = R10 = CHMe2) gave complete control of Haemonchus contortus in sheep at 5mg/kg orally.

L9 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1994:606025 CAPLUS

DN 121:206025

TI Preparation of cyclic depsipeptides with 18 ring atoms as **endoparasiticides**.

IN Jeschke, Peter; Scherkenbeck, Juergen; Bonse, Gerhard; Mencke, Norbert; **Harder, Achim**; Londershausen, Michael; Bischoff, Erwin; Mueller, Hartwig; Kurka, Peter

PA Bayer A.-G., Germany

SO Ger. Offen., 49 pp.
CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4317458	A1	19931216	DE 1993-4317458	19930526
	WO 9325543	A2	19931223	WO 1993-EP1436	19930607
	WO 9325543	A3	19940526		
	W: AU, BR, BY, CA, CZ, HU, JP, KR, KZ, NZ, RU, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9343236	A1	19940104	AU 1993-43236	19930607
	AU 668571	B2	19960509		
	EP 644883	A1	19950329	EP 1993-912908	19930607
	EP 644883	B1	19990915		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
	JP 07508723	T2	19950928	JP 1993-501102	19930607
	HU 73417	A2	19960729	HU 1994-3542	19930607
	AT 184598	E	19991015	AT 1993-912908	19930607
	ES 2137991	T3	20000101	ES 1993-912908	19930607
	CZ 286108	B6	20000112	CZ 1994-3106	19930607
	JP 3299752	B2	20020708	JP 1994-501102	19930607
	US 5821222	A	19981013	US 1996-728106	19961009
PRAI	DE 1992-4219157	A1	19920611		
	DE 1993-4317458	A	19930526		
	WO 1993-EP1436	A	19930607		
	US 1994-343517	B1	19941205		

OS MARPAT 121:206025

AB Title compds. [I; R1, R3, R5 = alkyl, hydroxyalkyl, alkoxyalkyl, mercaptoalkyl, alkylsulfinylalkyl, aminoalkyl, carbamoylalkyl,

guanidinoalkyl, alkenyl, cycloalkyl, (substituted) arylalkyl, etc.; R2, R4, R6 = alkyl, hydroxyalkyl, alkanoyloxyalkyl, alkoxyalkyl, aryloxyalkyl, alkylthioalkyl, carbamoylalkyl, aminoalkylsulfonyl, alkoxycarbonylaminoalkyl, alkenyl, cycloalkyl, (substituted) aryl, arylalkyl, etc.], were prepd. Thus, Z-MeIle-D-Lac-OH (MeIle = N-methylisoleucyl, Lac = lactyl) was coupled with H-(MeIle-D-Lac)2OBu-t in CH2Cl2 using (Me2CH)2NEt/BOP-Cl to give 77.4% Z-(MeIle-D-Lac)3OBu-t, which was O-deprotected with HCl in CH2Cl2 (82.9%) followed by coupling with pentafluorophenol using DCC in EtOAc to give 54% Z-(MeIle-D-Lac)3OPfp. This in dioxane was added over 6 h to a mixt. of Pd/C, 4-pyrrolidinopyridine, and EtOH in dioxane at 95.degree. under H to give 36.8% title compd. II. II was effective against Haemonchus contortus in sheep at 5 mg/kg.

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=> d his

     (FILE 'HOME' ENTERED AT 15:41:55 ON 23 JUL 2003)

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     LIFESCI, CAPLUS' ENTERED AT 15:42:05 ON 23 JUL 2003
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L1          139 S E3
                E VON SAMSON-HIMMELSTJERNA GEORG/AU
L2            2 S E4
                E VON SAMSON GEORG/AU
L3          149 S E2-E12
L4            2 S E23
L5          256 S L1-L4
L6           62 S L5 AND ENDOPARASIT?
L7           55 DUP REM L6 (7 DUPLICATES REMOVED)
L8            0 S L7 AND DEPSIDEPTIDE
L9           14 S L7 AND DEPSIPEPTIDE

=> s l7 and piperazine
L10           1 L7 AND PIPERAZINE

=> d bib ab

L10  ANSWER 1 OF 1  WPIDS  COPYRIGHT 2003 THOMSON DERWENT on STN
AN   2001-041784 [06]   WPIDS
DNC  C2001-012205
TI   Synergistic ectoparasiticide combination for use in human or veterinary
     medicine, comprising cyclic depsipeptide and piperazine compound
     as potentiating agent.
DC   B03 C02
IN   HARDER, A; SAMSON-HIMMELSTJERNA, G; VON SAMSON-HIMMELSTJERNA, G
PA   (FARB) BAYER AG
CYC  93
PI   DE 19921887   A1 20001116 (200106)*      15p
     WO 2000069425 A2 20001123 (200106)  DE
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
            OA PT SD SE SL SZ TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
            EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
            LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
            SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
     AU 2000055237 A  20001205 (200113)
     BR 2000010499 A  20020213 (200220)
     NO 2001005398 A  20011105 (200222)
     SK 2001001626 A3 20020305 (200225)
     EP 1189615    A2 20020327 (200229)  DE
         R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
```

RO SE SI
KR 2001109527 A 20011210 (200237)
CZ 2001004060 A3 20020612 (200251)
CN 1352559 A 20020605 (200261)
HU 2002001201 A2 20020828 (200264)
ZA 2001008238 A 20021224 (200309) 51p
JP 2002544224 W 20021224 (200313) 46p
ADT DE 19921887 A1 DE 1999-19921887 19990512; WO 2000069425 A2 WO 2000-EP4014 20000504; AU 2000055237 A AU 2000-55237 20000504; BR 2000010499 A BR 2000-10499 20000504, WO 2000-EP4014 20000504; NO 2001005398 A WO 2000-EP4014 20000504, NO 2001-5398 20011105; SK 2001001626 A3 WO 2000-EP4014 20000504, SK 2001-1626 20000504; EP 1189615 A2 EP 2000-940235 20000504, WO 2000-EP4014 20000504; KR 2001109527 A KR 2001-713555 20011023; CZ 2001004060 A3 WO 2000-EP4014 20000504, CZ 2001-4060 20000504; CN 1352559 A CN 2000-807450 20000504; HU 2002001201 A2 WO 2000-EP4014 20000504, HU 2002-1201 20000504; ZA 2001008238 A ZA 2001-8238 20011008; JP 2002544224 W JP 2000-617884 20000504, WO 2000-EP4014 20000504
FDT AU 2000055237 A Based on WO 200069425; BR 2000010499 A Based on WO 200069425; SK 2001001626 A3 Based on WO 200069425; EP 1189615 A2 Based on WO 200069425; CZ 2001004060 A3 Based on WO 200069425; HU 2002001201 A2 Based on WO 200069425; JP 2002544224 W Based on WO 200069425
PRAI DE 1999-19921887 19990512
AB DE 19921887 A UPAB: 20021105
NOVELTY - The use of **piperazine** derivatives (I) is claimed for potentiating the **endoparasitic** activity of cyclic depsipeptides (II), consisting of aminoacids and hydroxycarboxylic acids as ring components and having 24 ring atoms.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
(i) **endoparasitic** compositions containing (I) and (II); and
(ii) the use of (I) together with (II) for the preparation of **endoparasitic** compositions.
ACTIVITY - Anthelmintic.
In tests against Heterakis spumosa in mice, **piperazine** (Ia) at 4 x 250 mg/kg alone or 'depsipeptide I' (IIa) (see WO9325543) at 4 x 1 mg/kg alone gave 50-75% worm reduction, whereas a combination of (Ia) at 4 x 250 mg/kg and (IIa) at 4 x 1 mg/kg gave complete (more than 90%) worm reduction.
MECHANISM OF ACTION - None given.
USE - The combinations of (I) and (II) are useful in human or veterinary medicine for controlling pathogenic **endoparasites**, specifically cestodes, trematodes, nematodes or acanthocephalae. Activity is demonstrated in tests against Trichinella spiralis in vitro and against Heterakis spumosa or Nematospiroides dibius in mice.
ADVANTAGE - The combination of (I) and (II) (both known ectoparasiticides) has synergistic action, due to potentiation of the activity of (II) by (I).
Dwg.0/0

=> s depsipeptide and piperazine
6 FILES SEARCHED...
L11 11 DEPSIPEPTIDE AND PIPERAZINE

=> dup rem l11
PROCESSING COMPLETED FOR L11
L12 7 DUP REM L11 (4 DUPLICATES REMOVED)

=> d bib ab 1-7

L12 ANSWER 1 OF 7 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
AN 2002064650 EMBASE
TI Isolation of a novel cyclic hexadepsipeptide pipalamycin from Streptomyces as an apoptosis-inducing agent.

AU Uchihata Y.; Ando N.; Ikeda Y.; Kondo S.; Hamada M.; Umezawa K.
CS K. Umezawa, Department of Applied Chemistry, Faculty of Science and Technology, Keio University, 3-14-1 Hiyoshi, Kohoku-ku, Yokohama 223-0061, Japan. umezawa@applc.keio.ac.jp
SO Journal of Antibiotics, (2002) 55/1 (1-5).
Refs: 7
ISSN: 0021-8820 CODEN: JANTAJ
CY Japan
DT Journal; Article
FS 004 Microbiology
016 Cancer
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB The novel cyclic hexadepsipeptide named pipalamycin was isolated from a culture filtrate of Streptomyces sp. ML297-90F8 as an apoptosis-inducing agent. The antibiotic was found to be consisting of each one mole of alanine, N-hydroxyalanine, glycine, N-acylated 3-hydroxyleucine, and two moles of piperazic acid. Pipalamycin induced apoptosis in apoptosis-resistant human pancreatic adenocarcinoma AsPC-1 cells at 0.3 .mu.g/ml in 24-48 hours. It also showed antibacterial activity on Gram-positive bacteria such as Staphylococcus aureus and Micrococcus luteus. Fermentation, isolation, structural elucidation and the biological activities of pipalamycin are described.

L12 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:104442 CAPLUS
DN 134:266216
TI Morpholine-2,5-diones - their preparation and uses
AU Vinsova, Jarmila
CS Fac. Pharmacy, Charles Univ., Hradec Kralove, 500 05, Czech Rep.
SO Chemicke Listy (2001), 95(1), 22-27
CODEN: CHLSAC; ISSN: 0009-2770
PB Ceska Spolecnost Chemicka
DT Journal; General Review
LA Czech
AB Morpholine-2,5-diones are **depsipeptide** analogs of cyclic dipeptides, derivs. of **piperazine**-2,5-diones. In contrast to cyclodipeptides, which are formed by spontaneous cyclization, prepn. of cyclodidepsipeptides is not easy. Two main ways are used for cyclization of depsipeptides. Cyclization by the formation of ester bond seems more efficient than cyclization via the amide bond formation. The review with 51 refs. deals briefly with all known methods of syntheses of morpholine-2,5-diones but attention is also paid to their biol. activity. They are of great interest for biomedical applications. Optically active morpholine-2,5-diones are used as monomers for synthesis of biodegradable polymers, as prodrugs of bioactive amino acids and, most recently, in drug delivery systems.

L12 ANSWER 3 OF 7 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STNDUPLICATE 1
AN 2001-041784 [06] WPIDS
DNC C2001-012205
TI Synergistic ectoparasiticide combination for use in human or veterinary medicine, comprising cyclic **depsipeptide** and **piperazine** compound as potentiating agent.
DC B03 C02
IN HARDER, A; SAMSON-HIMMELSTJERNA, G; VON SAMSON-HIMMELSTJERNA, G
PA (FARB) BAYER AG
CYC 93
PI DE 19921887 A1 20001116 (200106)* 15p
WO 2000069425 A2 20001123 (200106) DE
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000055237 A 20001205 (200113)
BR 2000010499 A 20020213 (200220)
NO 2001005398 A 20011105 (200222)
SK 2001001626 A3 20020305 (200225)
EP 1189615 A2 20020327 (200229) DE
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI
KR 2001109527 A 20011210 (200237)
CZ 2001004060 A3 20020612 (200251)
CN 1352559 A 20020605 (200261)
HU 2002001201 A2 20020828 (200264)
ZA 2001008238 A 20021224 (200309) 51p
JP 2002544224 W 20021224 (200313) 46p

ADT DE 19921887 A1 DE 1999-19921887 19990512; WO 2000069425 A2 WO 2000-EP4014 20000504; AU 2000055237 A AU 2000-55237 20000504; BR 2000010499 A BR 2000-10499 20000504, WO 2000-EP4014 20000504; NO 2001005398 A WO 2000-EP4014 20000504, NO 2001-5398 20011105; SK 2001001626 A3 WO 2000-EP4014 20000504, SK 2001-1626 20000504; EP 1189615 A2 EP 2000-940235 20000504, WO 2000-EP4014 20000504; KR 2001109527 A KR 2001-713555 20011023; CZ 2001004060 A3 WO 2000-EP4014 20000504, CZ 2001-4060 20000504; CN 1352559 A CN 2000-807450 20000504; HU 2002001201 A2 WO 2000-EP4014 20000504, HU 2002-1201 20000504; ZA 2001008238 A ZA 2001-8238 20011008; JP 2002544224 W JP 2000-617884 20000504, WO 2000-EP4014 20000504

FDT AU 2000055237 A Based on WO 200069425; BR 2000010499 A Based on WO 200069425; SK 2001001626 A3 Based on WO 200069425; EP 1189615 A2 Based on WO 200069425; CZ 2001004060 A3 Based on WO 200069425; HU 2002001201 A2 Based on WO 200069425; JP 2002544224 W Based on WO 200069425

PRAI DE 1999-19921887 19990512

AB DE 19921887 A UPAB: 20021105

NOVELTY - The use of **piperazine** derivatives (I) is claimed for potentiating the endoparasitic activity of cyclic depsipeptides (II), consisting of aminoacids and hydroxycarboxylic acids as ring components and having 24 ring atoms.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
(i) endoparasitic compositions containing (I) and (II); and
(ii) the use of (I) together with (II) for the preparation of endoparasitic compositions.

ACTIVITY - Anthelmintic.

In tests against Heterakis spumosa in mice, **piperazine** (Ia) at 4 x 250 mg/kg alone or '**depsipeptide** I' (IIa) (see WO9325543) at 4 x 1 mg/kg alone gave 50-75% worm reduction, whereas a combination of (Ia) at 4 x 250 mg/kg and (IIa) at 4 x 1 mg/kg gave complete (more than 90%) worm reduction.

MECHANISM OF ACTION - None given.

USE - The combinations of (I) and (II) are useful in human or veterinary medicine for controlling pathogenic endoparasites, specifically cestodes, trematodes, nematodes or acanthocephalae. Activity is demonstrated in tests against Trichinella spiralis in vitro and against Heterakis spumosa or Nematospiroides dibius in mice.

ADVANTAGE - The combination of (I) and (II) (both known ectoparasiticides) has synergistic action, due to potentiation of the activity of (II) by (I).

Dwg.0/0

L12 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:587076 CAPLUS
DN 133:193492
TI Preparation of cyclopeptides or cyclic depsipeptides as antifungal agents

IN Barett, David; Tanaka, Akira; Okitsu, Osamu; Harada, Keiko; Ohki, Hidenori; Yamanaka, Hideaki; Kawabata, Koji
PA Fujisawa Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 300 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2000229998	A2	20000822	JP 1999-301639	19991022
PRAI JP 1998-368524	A	19981208		

OS MARPAT 133:193492
AB The title compds. [I; R1 = H, alkyl, lower alkoxyalkyl, CO2H, (un)substituted CONH2, aryl, lower (ar)alkyl, or heterocyclic carbonyl; R2 = (un)protected CO2H, (un)substituted heterocyclic carbonyl, (un)substituted NH2, N+(R5)3.X-; wherein R5 = (un)substituted lower alkyl or alkenyl; X = acid residue; R11 = HO, (un)substituted lower alkoxy; R12 = H, halo; R13 = H, NO2, NH2, acylamino; or R11 and R13 are bonded together to form O-CONH or -O-C-CONH; R14 = cyano, (un)substituted CONH2, (un)protected lower aminoalkyl; Z = O, NH, alkyl-N; P = (CH2)n; n = 0,1], which inhibit the biosynthesis of .alpha.-1,3-glucan and are useful for the treatment or prevention of bacterial infection, e.g. pneumonia caused by Pneumocystis carinii, are prepd. Thus, I.HCl (R1 = tridecyl, R2-A = H2N(CH2)3, R11 = OH, R12 = R13 = H, R14 = H2NCO, P = CH2, Z = O) was condensed with Et formimidate hydrochloride in the presence of diisopropylethylamine in DMF at room temp. for 4 days to give I.HCl [R2-A = NH:CHNH(CH2)3; R1, R2, R11, R12, R13, R14, P, Z = same as above] which showed min. inhibitory concn. of 0.20 .mu.g/mL against Candida albicans (FP633).

L12 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2
AN 2001:32913 BIOSIS
DN PREV200100032913
TI Synergistic action of a cyclic **depsipeptide** and **piperazine** on nematodes.
AU Nicolay, Frank; Harder, Achim (1); von Samson-Himmelstjerna, Georg; Mehlhorn, Heinz
CS (1) Business Group Animal Health, Research and Development, Bayer AG, 51368, Leverkusen: achim.harder.ah@bayer-ag.de Germany
SO Parasitology Research, (December, 2000) Vol. 86, No. 12, pp. 982-992. print.
ISSN: 0932-0113.
DT Article
LA English
SL English
AB The present study describes the synergistic effects of the cyclic **depsipeptide** BAY 44-4400 and **piperazine** in the treatment against the nematodes Trichinella spiralis, Heligmosomoides polygyrus, and Heterakis spumosa. The in vitro anthelmintic activity of a combination of the two compounds (1.7 motility units) against T. spiralis larvae was significantly higher than the sum of the individual drug effects (1.3 motility units). With regard to the rate of expulsion of H. polygyrus worms from the intestine of infected mice, an additive effect was observed; **piperazine** alone exerted an efficacy of 54.4% and BAY 44-4400 alone, one of 44.4%, whereas the combination of these compounds had an efficacy of 97.5%. With regard to the expulsion of H. spumosa worms, the effect of the combination was more than 5 orders of magnitude greater than the sum of the effects of the single compounds, i.e., there was a considerable potentiation of the actions of BAY 44-4400 and **piperazine**. Moreover, the combination exerted a significantly higher degree of degenerative effects on the intestine and on the nerve

chords of H. spumosa as compared with the single compounds.

L12 ANSWER 6 OF 7 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
AN 2000027028 EMBASE
TI Enantioselective synthesis of protected forms of (3R,5R)-5-hydroxypiperazic acid useful for synthesis.
AU Depew K.M.; Kamenecka T.M.; Danishefsky S.J.
CS K.M. Depew, Laboratory for Bioorganic Chemistry, Sloan-Kettering Inst. for Can. Res., 1275 York Avenue, New York, NY 10021, United States
SO Tetrahedron Letters, (15 Jan 2000) 41/3 (289-292).
Refs: 34
ISSN: 0040-4039 CODEN: TELEAY
PUI S 0040-4039(99)01958-9
CY United Kingdom
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
AB Protected versions of (3R,5R)-5-hydroxypiperazic acid were synthesized enantioselectively in two novel ways. The first derives its chirality from D- glutamic acid while the second uses an Evans amination and a diastereoselective bromolactonization to establish the two chiral centers. Given that this amino acid is a component of several depsipeptides, these two routes enable the synthesis of multigram quantities of protected versions of 2.

L12 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:364874 BIOSIS
DN PREV200000364874
TI The effect of the cyclic **depsipeptide** Bay 44-44 is synergistically enhanced by the GABA agonist **piperazine** - indicating a new neuropharmacological action.
AU von Samson-Himmelstjerna, G. (1); Nicolay, F.; Harder, A. (1); Mehlhorn, H.
CS (1) Bayer AG, Leverkusen Germany
SO European Journal of Neuroscience, (2000) Vol. 12, No. Supplement 11, pp. 43. print.
Meeting Info.: Meeting of the Federation of European Neuroscience Societies Brighton, UK June 24-28, 2000
ISSN: 0953-816X.
DT Conference
LA English
SL English

=> s endoparasit? and depsipeptide
L13 33 ENDOPARASIT? AND DEPSIPEPTIDE

=> s l13 and synerg?
L14 4 L13 AND SYNERG?

=> d bib ab 1-4

L14 ANSWER 1 OF 4 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2001-041784 [06] WPIDS
DNC C2001-012205
TI **Synergistic** ectoparasiticide combination for use in human or veterinary medicine, comprising cyclic **depsipeptide** and piperazine compound as potentiating agent.
DC B03 C02
IN HARDER, A; SAMSON-HIMMELSTJERNA, G; VON SAMSON-HIMMELSTJERNA, G
PA (FARB) BAYER AG
CYC 93

PI DE 19921887 A1 20001116 (200106)* 15p
WO 2000069425 A2 20001123 (200106) DE
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000055237 A 20001205 (200113)
BR 2000010499 A 20020213 (200220)
NO 2001005398 A 20011105 (200222)
SK 2001001626 A3 20020305 (200225)
EP 1189615 A2 20020327 (200229) DE
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
KR 2001109527 A 20011210 (200237)
CZ 2001004060 A3 20020612 (200251)
CN 1352559 A 20020605 (200261)
HU 2002001201 A2 20020828 (200264)
ZA 2001008238 A 20021224 (200309) 51p
JP 2002544224 W 20021224 (200313) 46p

ADT DE 19921887 A1 DE 1999-19921887 19990512; WO 2000069425 A2 WO 2000-EP4014 20000504; AU 2000055237 A AU 2000-55237 20000504; BR 2000010499 A BR 2000-10499 20000504, WO 2000-EP4014 20000504; NO 2001005398 A WO 2000-EP4014 20000504, NO 2001-5398 20011105; SK 2001001626 A3 WO 2000-EP4014 20000504, SK 2001-1626 20000504; EP 1189615 A2 EP 2000-940235 20000504, WO 2000-EP4014 20000504; KR 2001109527 A KR 2001-713555 20011023; CZ 2001004060 A3 WO 2000-EP4014 20000504, CZ 2001-4060 20000504; CN 1352559 A CN 2000-807450 20000504; HU 2002001201 A2 WO 2000-EP4014 20000504, HU 2002-1201 20000504; ZA 2001008238 A ZA 2001-8238 20011008; JP 2002544224 W JP 2000-617884 20000504, WO 2000-EP4014 20000504

FDT AU 2000055237 A Based on WO 200069425; BR 2000010499 A Based on WO 200069425; SK 2001001626 A3 Based on WO 200069425; EP 1189615 A2 Based on WO 200069425; CZ 2001004060 A3 Based on WO 200069425; HU 2002001201 A2 Based on WO 200069425; JP 2002544224 W Based on WO 200069425

PRAI DE 1999-19921887 19990512

AB DE 19921887 A UPAB: 20021105

NOVELTY - The use of piperazine derivatives (I) is claimed for potentiating the **endoparasitic** activity of cyclic depsipeptides (II), consisting of aminoacids and hydroxycarboxylic acids as ring components and having 24 ring atoms.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(i) **endoparasitic** compositions containing (I) and (II); and

(ii) the use of (I) together with (II) for the preparation of **endoparasitic** compositions.

ACTIVITY - Anthelmintic.

In tests against Heterakis spumosa in mice, piperazine (Ia) at 4 x 250 mg/kg alone or '**depsipeptide** I' (IIa) (see WO9325543) at 4 x 1 mg/kg alone gave 50-75% worm reduction, whereas a combination of (Ia) at 4 x 250 mg/kg and (IIa) at 4 x 1 mg/kg gave complete (more than 90%) worm reduction.

MECHANISM OF ACTION - None given.

USE - The combinations of (I) and (II) are useful in human or veterinary medicine for controlling pathogenic **endoparasites**, specifically cestodes, trematodes, nematodes or acanthocephalae. Activity is demonstrated in tests against Trichinella spiralis in vitro and against Heterakis spumosa or Nematospiroides dibius in mice.

ADVANTAGE - The combination of (I) and (II) (both known ectoparasiticides) has **synergistic** action, due to potentiation of the activity of (II) by (I).

Dwg.0/0

L14 ANSWER 2 OF 4 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 1997-034097 [03] WPIDS
DNC C1997-010612
TI **Synergistic** endo-parasitic agent, e.g. for treatment of domestic pets - contains macrocyclic lactone, e.g. avermectin, cyclic-**depsipeptide** and opt. praciquantil or epsiprantel.
DC B03 C02
IN HARDER, A; HELPAP, B; JESCHKE, P; MENCKE, N; KOELBL, B
PA (FARB) BAYER AG
CYC 45
PI WO 9638165 A2 19961205 (199703)* DE 35p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL OA PT SE
W: AU BB BG BR BY CA CN CZ HU JP KR KZ LK MX NO NZ PL RO RU SK TR UA US
DE 19520275 A1 19961205 (199704) 18p
WO 9638165 A3 19970109 (199713)
AU 9659004 A 19961218 (199714)
ZA 9604473 A 19970430 (199723) 35p
NO 9705516 A 19980106 (199812)
EP 828506 A2 19980318 (199815) DE
R: AT BE CH DE DK ES FI FR GB GR IE IT LI NL PT SE
CZ 9703825 A3 19980318 (199817)
SK 9701599 A3 19980708 (199836)
NZ 309073 A 19981223 (199906)
IL 118518 A 19981227 (199907)
AU 703048 B 19990311 (199922)
HU 9900346 A2 19990628 (199931)
JP 11506438 W 19990608 (199933) 39p
BR 9608961 A 19990629 (199937)
MX 9709245 A1 19980301 (200002)
KR 99022094 A 19990325 (200023)
CZ 287290 B6 20001011 (200060)
US 6159932 A 20001212 (200067)
EP 828506 B1 20020227 (200215) DE
R: AT BE CH DE DK ES FI FR GB GR IE IT LI NL PT SE
DE 59608798 G 20020404 (200225)
TW 469133 A 20011221 (200254)
CN 1191489 A 19980826 (200275)
ES 2173284 T3 20021016 (200279)
ADT WO 9638165 A2 WO 1996-EP2170 19960520; DE 19520275 A1 DE 1995-19520275 19950602; WO 9638165 A3 WO 1996-EP2170 19960520; AU 9659004 A AU 1996-59004 19960520; ZA 9604473 A ZA 1996-4473 19960531; NO 9705516 A WO 1996-EP2170 19960520, NO 1997-5516 19971201; EP 828506 A2 EP 1996-916137 19960520, WO 1996-EP2170 19960520; CZ 9703825 A3 WO 1996-EP2170 19960520, CZ 1997-3825 19960520; SK 9701599 A3 WO 1996-EP2170 19960520, SK 1997-1599 19960520; NZ 309073 A NZ 1996-309073 19960520, WO 1996-EP2170 19960520; IL 118518 A IL 1996-118518 19960531; AU 703048 B AU 1996-59004 19960520; HU 9900346 A2 WO 1996-EP2170 19960520, HU 1999-346 19960520; JP 11506438 W JP 1996-536146 19960520, WO 1996-EP2170 19960520; BR 9608961 A BR 1996-8961 19960520, WO 1996-EP2170 19960520; MX 9709245 A1 MX 1997-9245 19971128; KR 99022094 A WO 1996-EP2170 19960520, KR 1997-708573 19971128; CZ 287290 B6 WO 1996-EP2170 19960520, CZ 1997-3825 19960520; US 6159932 A WO 1996-EP2170 19960520, US 1997-952356 19971119; EP 828506 B1 EP 1996-916137 19960520, WO 1996-EP2170 19960520; DE 59608798 G DE 1996-508798 19960520, EP 1996-916137 19960520, WO 1996-EP2170 19960520; TW 469133 A TW 1996-105513 19960510; CN 1191489 A CN 1996-195661 19960520; ES 2173284 T3 EP 1996-916137 19960520
FDT AU 9659004 A Based on WO 9638165; EP 828506 A2 Based on WO 9638165; CZ 9703825 A3 Based on WO 9638165; NZ 309073 A Based on WO 9638165; AU 703048 B Previous Publ. AU 9659004, Based on WO 9638165; HU 9900346 A2 Based on WO 9638165; JP 11506438 W Based on WO 9638165; BR 9608961 A Based on WO 9638165; KR 99022094 A Based on WO 9638165; CZ 287290 B6 Previous Publ. CZ 9703825, Based on WO 9638165; US 6159932 A Based on WO 9638165; EP 828506 B1 Based on WO 9638165; DE 59608798 G Based on EP 828506, Based on WO

9638165; ES 2173284 T3 Based on EP 828506
PRAI DE 1995-19520275 19950602
AB WO 9638165 A UPAB: 19970212

Endoparasitic agent comprises: a) at least one avermectin, ivermectin (22,23-dihydro-avermectin B1) or milbemycin macrocyclic lactone; b) a cyclic **depsipeptide** comprising amino acid and hydroxycarboxylic acid units and contg. 6-30 ring atoms; and opt. c) praziquantil or epsiprantel.

USE - The agent is useful for the treatment and prophylaxis of **endoparasite** infestations caused by filaria, cestodes, trematodes, nematodes and acantocephales in human beings and animals, including birds, fish and insects, eg. bees and silkworms.

ADVANTAGE - (a) and (b) exert a **synergistic** effect, which results in economical and ecological benefits as a result of a lower dosage regimen. Further, the agent is more effective than prior art agents, esp. in the control of nematodes which affect dogs and cats, partic. Dirofilaria immitis.

Dwg.0/0

L14 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:807726 CAPLUS
DN 133:359221
TI Piperazines for enhancement of cyclic **depsipeptide** **endoparasiticides**
IN Harder, Achim; Von Samson-Himmelstjerna, Georg
PA Bayer A.-G., Germany
SO Ger. Offen., 16 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19921887	A1	20001116	DE 1999-19921887	19990512
	WO 2000069425	A2	20001123	WO 2000-EP4014	20000504
	WO 2000069425	A3	20010315		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 2000010499	A	20020213	BR 2000-10499	20000504
	EP 1189615	A2	20020327	EP 2000-940235	20000504
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002544224	T2	20021224	JP 2000-617884	20000504
	NO 2001005398	A	20011105	NO 2001-5398	20011105
	HR 2001000918	A1	20030430	HR 2001-918	20011211
PRAI	DE 1999-19921887	A	19990512		
	WO 2000-EP4014	W	20000504		

AB The invention discloses the use of piperazines to increase the **endoparasiticidal** effect of cyclic depsipeptides (having amino acids and hydroxy acids as ring components and with 24 ring atoms) for **endoparasiticidal** medicaments.

L14 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:51502 CAPLUS
DN 126:84585
TI **Endoparasitic** drug combination

IN Mencke, Norbert; Harder, Achim; Jeschke, Peter; Helpap, Barbara
PA Bayer A.-G., Germany
SO Ger. Offen., 17 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19520275	A1	19961205	DE 1995-19520275	19950602
	TW 469133	B	20011221	TW 1996-85105513	19960510
	CA 2222680	AA	19961205	CA 1996-2222680	19960520
	WO 9638165	A2	19961205	WO 1996-EP2170	19960520
	WO 9638165	A3	19970109		
	W: AU, BB, BG, BR, BY, CA, CN, CZ, HU, JP, KR, KZ, LK, MX, NO, NZ, PL, RO, RU, SK, TR, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9659004	A1	19961218	AU 1996-59004	19960520
	AU 703048	B2	19990311		
	EP 828506	A2	19980318	EP 1996-916137	19960520
	EP 828506	B1	20020227		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
	CN 1191489	A	19980826	CN 1996-195661	19960520
	JP 11506438	T2	19990608	JP 1996-536146	19960520
	BR 9608961	A	19990629	BR 1996-8961	19960520
	CZ 287290	B6	20001011	CZ 1997-3825	19960520
	AT 213645	E	20020315	AT 1996-916137	19960520
	ES 2173284	T3	20021016	ES 1996-916137	19960520
	PL 184848	B1	20021231	PL 1996-323595	19960520
	IL 118518	A1	19981227	IL 1996-118518	19960531
	US 6159932	A	20001212	US 1997-952356	19971119
	NO 9705516	A	19980106	NO 1997-5516	19971201
PRAI	DE 1995-19520275	A	19950602		
	WO 1996-EP2170	W	19960520		

OS MARPAT 126:84585
AB A combination of a macrocyclic lactone (avermectin, ivermectin, or milbemycin) with a cyclic **depsipeptide**, optionally including praziquantel or epsiprantel, is useful as a **synergistic** nematocide for treatment of ascarid, hookworm, trichurid, and filarial infestations in mammals. Thus, a combination of PF 1022A (cyclic **depsipeptide**) 50.0 and ivermectin B1a/B1b 0.1 mg/kg orally was 100% effective against Nematospiroides dubius infestation in mice.

=> s parasit? and drug (5a) combin?
L15 5459 PARASIT? AND DRUG (5A) COMBIN?

=> s l15 and synerg?
L16 467 L15 AND SYNERG?

=> s l16 and (piperazine? or depsipeptid?
UNMATCHED LEFT PARENTHESIS 'AND (PIPERAZINE'
The number of right parentheses in a query must be equal to the number of left parentheses.

=> s l16 and (piperazine? or depsipeptid?)
L17 6 L16 AND (PIPERAZINE? OR DEPSIPEPTID?)

=> dup rem l17
PROCESSING COMPLETED FOR L17
L18 5 DUP REM L17 (1 DUPLICATE REMOVED)

=> d bib ab 1-5

L18 ANSWER 1 OF 5 CABA COPYRIGHT 2003 CABI on STN
AN 2001:31654 CABA
DN 20003026922
TI **Synergistic** action of a cyclic **depsipeptide** and **piperazine** on nematodes
AU Nicolay, F.; Harder, A.; Samson-Himmelstjerna, G. von; Mehlhorn, H.; von Samson-Himmelstjerna, G.
CS Institute of Zoomorphology, Cell Biology and Parasitology, Heinrich-Heine-University Dusseldorf, Universitatsstrasse 1, 40225 Dusseldorf, Germany.
SO Parasitology Research, (2000) Vol. 86, No. 12, pp. 982-992. 17 ref.
ISSN: 0932-0113
DT Journal
LA English
AB The **synergistic** effects of the cyclic **depsipeptide** BAY 44-4400 and **piperazine** in the treatment of Trichinella spiralis, Heligmosomoides polygyrus and Heterakis spumosa infections in mice were investigated. The in vitro anthelmintic activity of a combination of the 2 compounds (1.7 motility units) against T. spiralis larvae was significantly higher than the sum of the individual drug effects (1.3 motility units). With regard to the rate of expulsion of H. polygyrus worms from the intestine of infected mice, an additive effect was observed; **piperazine** and BAY 44-4400 alone exerted individual efficacies of 54.4 and 44.4%, respectively, whereas the combination of both compounds had an efficacy of 97.5%. With regard to the expulsion of H. spumosa worms, the effect of the combination was more than 5 orders of magnitude greater than the sum of the effects of the individual compounds, showing that there was a considerable potentiation of the actions of BAY 44-4400 and **piperazine**. The **drug combination** exerted a significantly higher degree of degenerative effects on the intestine and on the nerve cords of H. spumosa, compared with the individual compounds.

L18 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:147346 CAPLUS
DN 128:213381
TI Compositions and methods for treating infections using analogs of indolicidin
IN Fraser, Janet R.; West, Michael H. P.; Krieger, Timothy J.; Taylor, Robert; Erfle, Douglas
PA Micrologix Biotech, Inc., Can.; Fraser, Janet R.; West, Michael H. P.; Krieger, Timothy J.; Taylor, Robert; Erfle, Douglas
SO PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9807745	A2	19980226	WO 1997-US14779	19970821
	WO 9807745	A3	19980709		
	W: AL, AM, AT, AU, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9743279	A1	19980306	AU 1997-43279	19970821
	EP 925308	A2	19990630	EP 1997-941352	19970821

	EP 925308	B1	20020605			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 2001500477	T2	20010116	JP 1998-510994	19970821	
	EP 1174439	A2	20020123	EP 2001-119148	19970821	
	EP 1174439	A3	20030326			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	AT 218579	E	20020615	AT 1997-941352	19970821	
	ES 2178000	T3	20021216	ES 1997-941352	19970821	
PRAI	US 1996-24754P	P	19960821			
	US 1997-34949P	P	19970113			
	EP 1997-941352	A3	19970821			
	WO 1997-US14779	W	19970821			

OS MARPAT 128:213381

AB Compns. and methods for treating infections, esp. bacterial infections, are provided. Indolicidin peptide analogs contg. at least two basic amino acids are prepd. The analogs are administered as modified peptides, preferably contg. photo-oxidized solubilizer.

L18 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1997:51502 CAPLUS

DN 126:84585

TI Endoparasitic **drug combination**

IN Mencke, Norbert; Harder, Achim; Jeschke, Peter; Helpap, Barbara

PA Bayer A.-G., Germany

SO Ger. Offen., 17 pp.
CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19520275	A1	19961205	DE 1995-19520275	19950602
	TW 469133	B	20011221	TW 1996-85105513	19960510
	CA 2222680	AA	19961205	CA 1996-2222680	19960520
	WO 9638165	A2	19961205	WO 1996-EP2170	19960520
	WO 9638165	A3	19970109		
	W: AU, BB, BG, BR, BY, CA, CN, CZ, HU, JP, KR, KZ, LK, MX, NO, NZ, PL, RO, RU, SK, TR, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9659004	A1	19961218	AU 1996-59004	19960520
	AU 703048	B2	19990311		
	EP 828506	A2	19980318	EP 1996-916137	19960520
	EP 828506	B1	20020227		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
	CN 1191489	A	19980826	CN 1996-195661	19960520
	JP 11506438	T2	19990608	JP 1996-536146	19960520
	BR 9608961	A	19990629	BR 1996-8961	19960520
	CZ 287290	B6	20001011	CZ 1997-3825	19960520
	AT 213645	E	20020315	AT 1996-916137	19960520
	ES 2173284	T3	20021016	ES 1996-916137	19960520
	PL 184848	B1	20021231	PL 1996-323595	19960520
	IL 118518	A1	19981227	IL 1996-118518	19960531
	US 6159932	A	20001212	US 1997-952356	19971119
	NO 9705516	A	19980106	NO 1997-5516	19971201
PRAI	DE 1995-19520275	A	19950602		
	WO 1996-EP2170	W	19960520		

OS MARPAT 126:84585

AB A combination of a macrocyclic lactone (avermectin, ivermectin, or milbemycin) with a cyclic **depsipeptide**, optionally including praziquantel or epsiprantel, is useful as a **synergistic**

nematocide for treatment of ascarid, hookworm, trichurid, and filarial infestations in mammals. Thus, a combination of PF 1022A (cyclic **depsipeptide**) 50.0 and ivermectin B1a/B1b 0.1 mg/kg orally was 100% effective against Nematospiroides dubius infestation in mice.

L18 ANSWER 4 OF 5 CABA COPYRIGHT 2003 CABI on STN
AN 91:83681 CABA
DN 912227873
TI Efficacy of anthelmintics against mixed helminth infections in fowls
AU Hadykto, M. V.; Kulik, O. M.
CS Vsesoyuznyi Institut Vetpreparatov, Moscow, USSR.
SO Veterinariya (Moskva), (1991) No. 3, pp. 43-46. 12 ref.
ISSN: 0042-4846
DT Journal
LA Russian
SL English
AB In 200 hens carrying Ascaridia galli and Heterakis gallinae, the combined use of levamisole at 15 mg a head and **piperazine** at 150 mg a head, given on two consecutive days, had a **synergic** action. In 100 hens carying Ascaridia galli and unspecified cestodes, levamisole at 40 mg enhanced the cestocidal action of niclosamide at 200 mg a head.

L18 ANSWER 5 OF 5 MEDLINE on STN DUPLICATE 1
AN 78122168 MEDLINE
DN 78122168 PubMed ID: 629460
TI Anthelmintic efficacy of thenium closylate-**piperazine** phosphate combination tablets against Toxocara canis in pups and young dogs.
AU Corwin R M; Miller T A
SO AMERICAN JOURNAL OF VETERINARY RESEARCH, (1978 Feb) 39 (2) 263-5.
Journal code: 0375011. ISSN: 0002-9645.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197804
ED Entered STN: 19900314
Last Updated on STN: 19900314
Entered Medline: 19780426
AB Thenium closylate-**piperazine** phosphate combination tablets, tablets containing either thenium or **piperazine**, and control tablets (excipients only) were administered in 2 doses 5 to 7.5 hours apart to weaned pups and young dogs, in critical controlled trials to test efficacy against naturally acquired infections of Toxocara canis. In the 1st trial, the combination tablets produced a mean clearance of 94% from 18 pups. Tablets containing thenium alone showed a mean clearance of 9% from 25 pups, and tablets containing **piperazine** alone caused a mean clearance of 56% from 16 pups. Clearances, corrected for spontaneous worm losses observed in pups treated with the control tablets, were 90% (combination), 5% (thenium alone), and 52% (**piperazine** alone). In the 2nd and 3rd trials, efficacy of the combination tablet in 15 pups was 78% when corrected for worm losses in pups which had received placebo (excipient) tablets. Each component in the combination tablet contributed its full single-entity efficacy and, if in combination, **synergistic** effect between the components.

=> file biosis medline agricola embase caba wpids japio biotechds lifesci caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	185.40	185.61

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION

CA SUBSCRIBER PRICE -9.77 -9.77

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=> s bay 44-4400
L19 18 BAY 44-4400

=> dup rem l19
PROCESSING COMPLETED FOR L19
L20 4 DUP REM L19 (14 DUPLICATES REMOVED)

=> d bib ab 1-4

L20 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1
AN 2001:555185 BIOSIS
DN PREV200100555185
TI Filaricidal efficacy of anthelmintically active cyclodepsipeptides.
AU Zahner, Horst (1); Taubert, Anja; Harder, Achim; von Samson-Himmelstjerna, Georg
CS (1) Institute for Parasitology, Justus Liebig University Giessen, Rudolf-Buchheim-Strasse 2, D-35392, Giessen: horst.zahner@vetmed.uni-giessen.de Germany
SO International Journal for Parasitology, (November, 2001) Vol. 31, No. 13, pp. 1515-1522. print.
ISSN: 0020-7519.
DT Article
LA English
SL English
AB PF 1022A, a novel anthelmintically active cyclodepsipeptide, and **Bay 44-4400**, a semisynthetic derivative of PF 1022A were tested for filaricidal efficacy in Mastomys coucha infected with Litomosoides sigmodontis, Acanthocheilonema viteae and Brugia malayi. The parent compound PF 1022A showed limited anti-filarial efficacy in L.

sigmodontis and B. malayi infected animals. Oral doses of 5X100 mg/kg on consecutive days caused only a temporary decrease of microfilariaemia levels. By contrast, **Bay 44-4400** was highly effective against microfilariae of all three species in single oral, subcutaneous and cutaneously applied (spot on) doses. Minimum effective doses (MED, reducing parasitaemia density by gtoreq95%) determined 3 and 7 days after treatment were 3.125-6.25 and 6.25-12.5 mg/kg, respectively. Using the spot on formulation, doses of 6.25 mg/kg (L. sigmodontis), 12.5 mg/kg (A. viteae) and 25 mg/kg (B. malayi) were required to cause reductions of microfilaraemia levels by gtoreq95% until day 56. Adulticidal effects, determined as minimum curative doses (MCD, eliminating adult parasites within 56 days by >95%) after single dose treatment were limited to A. viteae (MCD, 100 mg/kg independent of the route of administration). Repeated oral treatment (100 mg/kg on 5 consecutive days) killed all adult L. sigmodontis but did not affect B. malayi. However, single doses of 6.25 and 25 mg/kg resulted in severe pathological alterations of intrauterine stages of L. sigmodontis and B. malayi, respectively. These alterations may be responsible for long-lasting reductions of microfilaraemia even when curative effects could not be achieved.

L20 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2
AN 2002:271147 BIOSIS
DN PREV200200271147
TI Activity of the cyclic depsipeptide emodepside (**BAY 44 -4400**) against larval and adult stages of nematodes in rodents and the influence on worm survival.
AU Harder, Achim (1); von Samson-Himmelstjerna, Georg
CS (1) Business Group Animal Health, Research and Development, Biological Chemical Evaluation, Bayer AG, Alfred-Nobel-Strasse 50, 40789, Monheim: achim.harder.ah@bayer-ag.de Germany
SO Parasitology Research, (November, 2001) Vol. 87, No. 11, pp. 924-928. print.
ISSN: 0932-0113.
DT Article
LA English
AB The present investigations deal with the activity of the cyclic depsipeptide emodepside (**BAY 44-4400**) against larval and adult stages of three rodent nematodes. While emodepside acts strongly against the adult stages of the rat nematodes Nippostrongylus brasiliensis and Strongyloides ratti, as well as against the mouse nematode Heligmosomoides polygyrus, its actions against the larval stages of these nematodes vary according to the species. Thus, emodepside is highly effective against the lung and intestine larval stages of N. brasiliensis and S. ratti. By contrast, the larval stages of H. polygyrus in the intestine are only partly affected by higher emodepside dosages.

L20 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 3
AN 2001:478778 BIOSIS
DN PREV200100478778
TI Effects of **Bay 44-4400**, a new cyclodepsipeptide, on developing stages of filariae (Acanthocheilonema viteae, Brugia malayi, Litomosoides sigmodontis) in the rodent Mastomys coucha.
AU Zahner, H. (1); Taubert, Anja; Harder, Achim; von Samson-Himmelstjerna, Georg
CS (1) Institute of Parasitology, Justus Liebig University Giessen, Rudolf-Buchheim-Strasse 2, D-35392, Giessen: horst.zahner@vetmed.uni-giessen.de Germany
SO Acta Tropica, (1 September, 2001) Vol. 80, No. 1, pp. 19-28. print.

ISSN: 0001-706X.
DT Article
LA English
SL English
AB **Bay 44-4400** was used as a spot on formulation and administered in single doses of 25 and 100 mg/kg to Acanthocheilonema viteae, Brugia malayi, and Litomosoides sigmodontis infected Mastomys coucha on various dates during prepatency, aiming to affect third stage larvae, fourth stage larvae or preadult worms. Microfilaraemia levels were controlled in comparison to untreated controls until necropsies were performed 100 days p.i. (A. viteae, L. sigmodontis) and 150 days p.i. (B. malayi) to determine the numbers of surviving worms and the condition of intrauterine developing stages. A significant proportion (86-100%) of larval and preadult stages of A. viteae were killed by **Bay 44-4400** at a dose of 100 mg/kg. A dose of 25 mg/kg had only insignificant effects on the developing parasites, however, it strongly reduced microfilaraemia levels caused by surviving worms in the early phase of patency. Larval and preadult B. malayi and L. sigmodontis were not killed by **Bay 44-4400** to a significant degree. Microfilaraemia developing by surviving parasites was generally and significantly reduced throughout the observation period when treatment was performed to affect the preadult parasites. In the other cases variable results were obtained. Intrauterine early embryonic stages were found to be pathologically altered in worms which had been treated at a preadult stage.

L20 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 4
AN 2001:32913 BIOSIS
DN PREV200100032913
TI Synergistic action of a cyclic depsipeptide and piperazine on nematodes.
AU Nicolay, Frank; Harder, Achim (1); von Samson-Himmelstjerna, Georg; Mehlhorn, Heinz
CS (1) Business Group Animal Health, Research and Development, Bayer AG, 51368, Leverkusen: achim.harder.ah@bayer-ag.de Germany
SO Parasitology Research, (December, 2000) Vol. 86, No. 12, pp. 982-992. print.
ISSN: 0932-0113.
DT Article
LA English
SL English
AB The present study describes the synergistic effects of the cyclic depsipeptide **BAY 44-4400** and piperazine in the treatment against the nematodes Trichinella spiralis, Heligmosomoides polygyrus, and Heterakis spumosa. The in vitro anthelmintic activity of a combination of the two compounds (1.7 motility units) against T. spiralis larvae was significantly higher than the sum of the individual drug effects (1.3 motility units). With regard to the rate of expulsion of H. polygyrus worms from the intestine of infected mice, an additive effect was observed; piperazine alone exerted an efficacy of 54.4% and **BAY 44-4400** alone, one of 44.4%, whereas the combination of these compounds had an efficacy of 97.5%. With regard to the expulsion of H. spumosa worms, the effect of the combination was more than 5 orders of magnitude greater than the sum of the effects of the single compounds, i.e., there was a considerable potentiation of the actions of **BAY 44-4400** and piperazine. Moreover, the combination exerted a significantly higher degree of degenerative effects on the intestine and on the nerve chords of H. spumosa as compared with the single compounds.

=> dhis
DHIS IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

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=> d his

     (FILE 'HOME' ENTERED AT 15:41:55 ON 23 JUL 2003)

     FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
     LIFESCI, CAPLUS' ENTERED AT 15:42:05 ON 23 JUL 2003
                E HARDER ACHIM/AU
L1          139 S E3
                E VON SAMSON-HIMMELSTJERNA GEORG/AU
L2            2 S E4
                E VON SAMSON GEORG/AU
L3          149 S E2-E12
L4            2 S E23
L5          256 S L1-L4
L6           62 S L5 AND ENDOPARASIT?
L7           55 DUP REM L6 (7 DUPLICATES REMOVED)
L8            0 S L7 AND DEPSIDEPTIDE
L9           14 S L7 AND DEPSIPEPTIDE
L10           1 S L7 AND PIPERAZINE
L11          11 S DEPSIPEPTIDE AND PIPERAZINE
L12           7 DUP REM L11 (4 DUPLICATES REMOVED)
L13          33 S ENDOPARASIT? AND DEPSIPEPTIDE
L14           4 S L13 AND SYNERG?
L15        5459 S PARASIT? AND DRUG (5A) COMBIN?
L16         467 S L15 AND SYNERG?
L17           6 S L16 AND (PIPERAZINE? OR DEPSIPEPTID?)
L18           5 DUP REM L17 (1 DUPLICATE REMOVED)

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     LIFESCI, CAPLUS' ENTERED AT 16:09:00 ON 23 JUL 2003
L19          18 S BAY 44-4400
L20           4 DUP REM L19 (14 DUPLICATES REMOVED)

=> s l19 and piperazine
L21           4 L19 AND PIPERAZINE

=> d ti 1-4

L21  ANSWER 1 OF 4  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
TI   Synergistic action of a cyclic depsipeptide and piperazine on
     nematodes.

L21  ANSWER 2 OF 4     MEDLINE on STN
TI   Synergistic action of a cyclic depsipeptide and piperazine on
     nematodes.

L21  ANSWER 3 OF 4  EMBASE  COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
TI   Synergistic action of a cyclic depsipeptide and piperazine on
     nematodes.

L21  ANSWER 4 OF 4  CABA COPYRIGHT 2003 CABI on STN
TI   Synergistic action of a cyclic depsipeptide and piperazine on
     nematodes.


=> d bib ab

L21  ANSWER 1 OF 4  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN   2001:32913  BIOSIS
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DN PREV200100032913
TI Synergistic action of a cyclic depsipeptide and **piperazine** on nematodes.
AU Nicolay, Frank; Harder, Achim (1); von Samson-Himmelstjerna, Georg; Mehlhorn, Heinz
CS (1) Business Group Animal Health, Research and Development, Bayer AG, 51368, Leverkusen: achim.harder.ah@bayer-ag.de Germany
SO Parasitology Research, (December, 2000) Vol. 86, No. 12, pp. 982-992. print.
ISSN: 0932-0113.
DT Article
LA English
SL English
AB The present study describes the synergistic effects of the cyclic depsipeptide **BAY 44-4400** and **piperazine** in the treatment against the nematodes Trichinella spiralis, Heligmosomoides polygyrus, and Heterakis spumosa. The in vitro anthelmintic activity of a combination of the two compounds (1.7 motility units) against T. spiralis larvae was significantly higher than the sum of the individual drug effects (1.3 motility units). With regard to the rate of expulsion of H. polygyrus worms from the intestine of infected mice, an additive effect was observed; **piperazine** alone exerted an efficacy of 54.4% and **BAY 44-4400** alone, one of 44.4%, whereas the combination of these compounds had an efficacy of 97.5%. With regard to the expulsion of H. spumosa worms, the effect of the combination was more than 5 orders of magnitude greater than the sum of the effects of the single compounds, i.e., there was a considerable potentiation of the actions of **BAY 44-4400** and **piperazine**. Moreover, the combination exerted a significantly higher degree of degenerative effects on the intestine and on the nerve chords of H. spumosa as compared with the single compounds.

=> s pf1022a
L22 135 PF1022A

=> s l22 and piperazine
L23 0 L22 AND PIPERAZINE

=> s l22 and synerg?
L24 2 L22 AND SYNERG?

=> d bib ab 1-2

L24 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1992:430273 BIOSIS
DN BA94:82398
TI NEUROPHARMACOLOGICAL MECHANISM OF ACTION OF **PF1022A** AN ANTINEMATODE ANTHELMINTIC WITH A NEW STRUCTURE OF CYCLIC DEPSIPEPTIDE ON ANGIOSTRONGYLUS-CANTONENSIS AND ISOLATED FROG RECTUS.
AU TERADA M
CS DEP. PARASITOL., HAMAMATSU UNIV. SCH. MED., 3600 HANDA-CHO, HAMAMATSU 431-31, JPN.
SO JPN J PARASITOL, (1992) 41 (2), 108-117.
CODEN: KISZAR. ISSN: 0021-5171.
FS BA; OLD
LA English
AB Mechanism of action of **PF1022A** was studied neuropharmacologically. Against Angiostrongylus cantonensis, **PF1022A** inhibited the motility at such a low concentration as 10-13 g/ml, and paralyzed the worm at 10-12-10-6 g/ml. The paralysis by the drug at 10-12 g/ml was partially antagonized by gabergic antagonists like picrotoxin and bicuculline, and completely reversed when

N-methylcytisine (N-MC) was added with gabergic antagonists. On the other hand, in the preparations paralyzed by PF1022A (10-**10** g/ml), the spasmogenic effects of N-MC and eserine were kept inhibited even with gabergic antagonists, while those of pyrantel were not inhibited. Paralysis by PF1022A (10-**12** g/ml) was antagonized by Ca2+ combined with gabergic antagonists. The reversed motility by Ca2+ was again paralyzed by the addition of PF1022A (10-**10** g/ml). The guanidine (2.5 .times. 10-3 M)-induced twitch response in the isolated frog rectus with or without N-MC was inhibited PF1022A (10-**6** g/ml), while contraction by pyrantel was not inhibited in the paralyzed preparation. From these results, it is suggested that PF1022A affects **neuropharmacologically** the nematode and the frog rectus. And in A. cantonensis, the inhibition is produced synergistically by **stimulating** the gabergic mechanism and inhibiting the cholinergic mechanism. As the drug is extremely less toxic against host animals, it is quite likely that PF1022A becomes **available** as a superior antinematode drug.

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TI Neuropharmacological mechanism of action of **Pf1022A**, an antinematode anthelmintic with a new structure of cyclic depsipeptide, on Angiostrongylus cantonensis and isolated frog rectus
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DT Journal
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AB The mechanism of action of **PF1022A** was studied neuropharmacologically. **PF1022A** inhibited motility in A. cantonensis at a concentration of 10-13 g/ml, and paralysed the worm at 10-12-10-6 g/ml. Paralysis by the drug at 10-12 g/ml was partially antagonized by gabergic antagonists like picrotoxin and bicuculline, and completely reversed when N-methylcytisine (N-MC) was added with gabergic antagonists. However in the preparations paralysed by PF1022A (10-**10** g/ml), the spasmogenic effects of N-MC and eserine were kept inhibited even with gabergic antagonists, while those of pyrantel were not inhibited. Paralysis by PF1022A (10-**12** g/ml) was antagonized by Ca2+ combined with gabergic antagonists. The reversed motility by Ca2+ was again paralysed by the addition of PF1022A (10-**10** g/ml). The guanidine (2.5 x 10-13 M)-induced twitch response in the isolated frog rectus with or without N-MC was inhibited by PF1022A (10-**6** g/ml), while contraction by pyrantel was not inhibited in the paralysed preparation. It is suggested that PF1022A affects **neuropharmacologically** the nematode and the frog rectus, and in A. cantonensis, the inhibition is produced synergistically by **stimulating** the gabergic mechanism and inhibiting the cholinergic mechanism. As the drug has a low toxicity against host animals it is thought likely that PF1022A will **become** available as a superior antinematode drug.